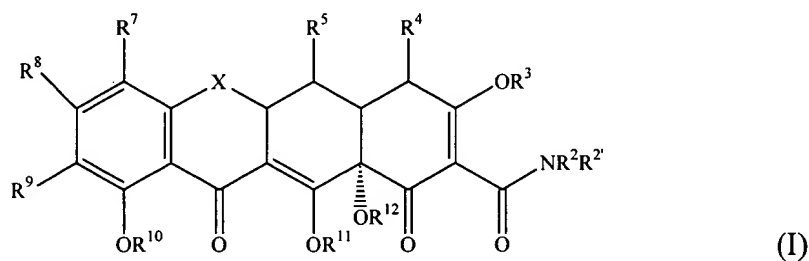


### Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

### Listing of Claims:

Claim 1 (currently amended): A substituted tetracycline compound of Formula I:



wherein:

X is  $\text{CHC}(\text{R}^{13}\text{Y}'\text{Y})$ ,  $\text{CR}^{6'}\text{R}^6$ ,  $\text{C}=\text{CR}^{6'}\text{R}^6$ , S,  $\text{NR}^6$ , or O;

$\text{R}^2$ ,  $\text{R}^{2'}$ ,  $\text{R}^4$ , and  $\text{R}^{4'}$  are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$\text{R}^4$  is  $\text{NR}^{4'}\text{R}^{4''}$ , alkyl, alkenyl, alkynyl, aryl, hydroxyl, halogen, or hydrogen;

$\text{R}^{2'}$ ,  $\text{R}^3$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$  and  $\text{R}^{12}$  are each hydrogen or a pro-drug moiety;

$\text{R}^5$  is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$\text{R}^6$  and  $\text{R}^{6'}$  are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

$\text{R}^7$  is ~~nitro, alkyl, alkenyl, alkynyl substituted with an aryl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, or~~  $(\text{CH}_2)_{0-3}\text{NR}^{7e}\text{C}(=\text{W}')\text{WR}^{7a}$ ;

$\text{R}^9$  is hydrogen, ~~nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, thionitroso(e.g.,~~  $\text{N}=\text{S})$ , or  $(\text{CH}_2)_{0-3}\text{NR}^{9e}\text{C}(=\text{Z}')\text{ZR}^{9a}$ ;

~~\_\_\_\_\_~~  $\text{Z}$  is  $\text{CR}^{9d}\text{R}^{9e}$ , S,  $\text{NR}^{9b}$  or O;

~~\_\_\_\_\_~~  $\text{Z}'$  is O, S, or  $\text{NR}^{9f}$ ;

~~\_\_\_\_\_~~  $\text{W}$  is  $\text{CR}^{7d}\text{R}^{7e}$ , S,  $\text{NR}^{7b}$  or O;

~~\_\_\_\_\_~~  $\text{W}'$  is O,  $\text{NR}^{7f}$  S;

~~R<sup>7a</sup>, R<sup>7b</sup>, R<sup>7c</sup>, R<sup>7d</sup>, R<sup>7e</sup>, R<sup>9a</sup>, R<sup>9b</sup>, R<sup>9c</sup>, R<sup>9d</sup>, and R<sup>9e</sup> are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;~~

R<sup>8</sup> is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R<sup>13</sup> is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl, and pharmaceutically acceptable salts thereof.

Claim 2 (currently amended): The tetracycline compound of claim 1, wherein R<sup>4</sup> is NR<sup>4'</sup>R<sup>4''</sup>, X is CR<sup>6</sup>R<sup>6'</sup>; R<sup>2</sup>, R<sup>2'</sup>, R<sup>6</sup>, R<sup>6'</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are each hydrogen; R<sup>4'</sup> and R<sup>4''</sup> are lower alkyl; and R<sup>5</sup> is hydroxy or hydrogen.

Claim 3 (original): The tetracycline compound of claim 2, wherein R<sup>4'</sup> and R<sup>4''</sup> are each methyl and R<sup>5</sup> is hydrogen.

Claims 4-52 (cancelled).

Claim 53 (currently amended): The tetracycline compound of claim ~~3~~52, wherein said substituted alkynyl is substituted with substituted or unsubstituted phenyl.

Claim 54 (original): The tetracycline compound of claim 53, wherein said substituted phenyl is substituted with one or more substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, carboxy, alkylcarbonylamino, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, amino, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl and heteroaryl.

Claim 55 (original): The tetracycline compound of claim 54, wherein said phenyl is substituted with alkylcarbonylamino or sulphonamido.

$$\begin{array}{c}
 \text{R}^7 \quad \text{R}^5 \quad \text{R}^4 \\
 | \quad | \quad | \\
 \text{R}^8 \quad \text{X} \quad \text{OR}^3 \\
 | \quad | \quad | \\
 \text{R}^9 \quad \text{OR}^{10} \quad \text{C=O} \quad \text{OR}^{11} \quad \text{OR}^{12} \quad \text{C=O} \quad \text{NR}^2\text{R}^{2'} \\
 | \quad | \quad | \quad | \quad | \quad | \\
 \text{OR}^{10} \quad \text{C=O} \quad \text{OR}^{11} \quad \text{OR}^{12} \quad \text{C=O} \quad \text{C=O}
 \end{array}
 \quad (I)$$

X is  $\text{CHC}(\text{R}^{13}\text{Y}'\text{Y})$ ,  $\text{CR}^6\text{R}^6$ ,  $\text{C}=\text{CR}^6\text{R}^6$ , S,  $\text{NR}^6$ , or O;

$\text{R}^2$ ,  $\text{R}^{2'}$ ,  $\text{R}^4$ , and  $\text{R}^{4''}$  are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$\text{R}^4$  is  $\text{NR}^{4'}\text{R}^{4''}$ , alkyl, alkenyl, alkynyl, aryl, hydroxyl, halogen, or hydrogen;

$\text{R}^{2'}$ ,  $\text{R}^3$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$  and  $\text{R}^{12}$  are each hydrogen or a pro-drug moiety;

$\text{R}^5$  is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$\text{R}^6$  and  $\text{R}^{6'}$  are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

$\text{R}^7$  is substituted alkynyl, wherein said substituted alkynyl is substituted with a tetracycline moiety;

$\text{R}^9$  is hydrogen;

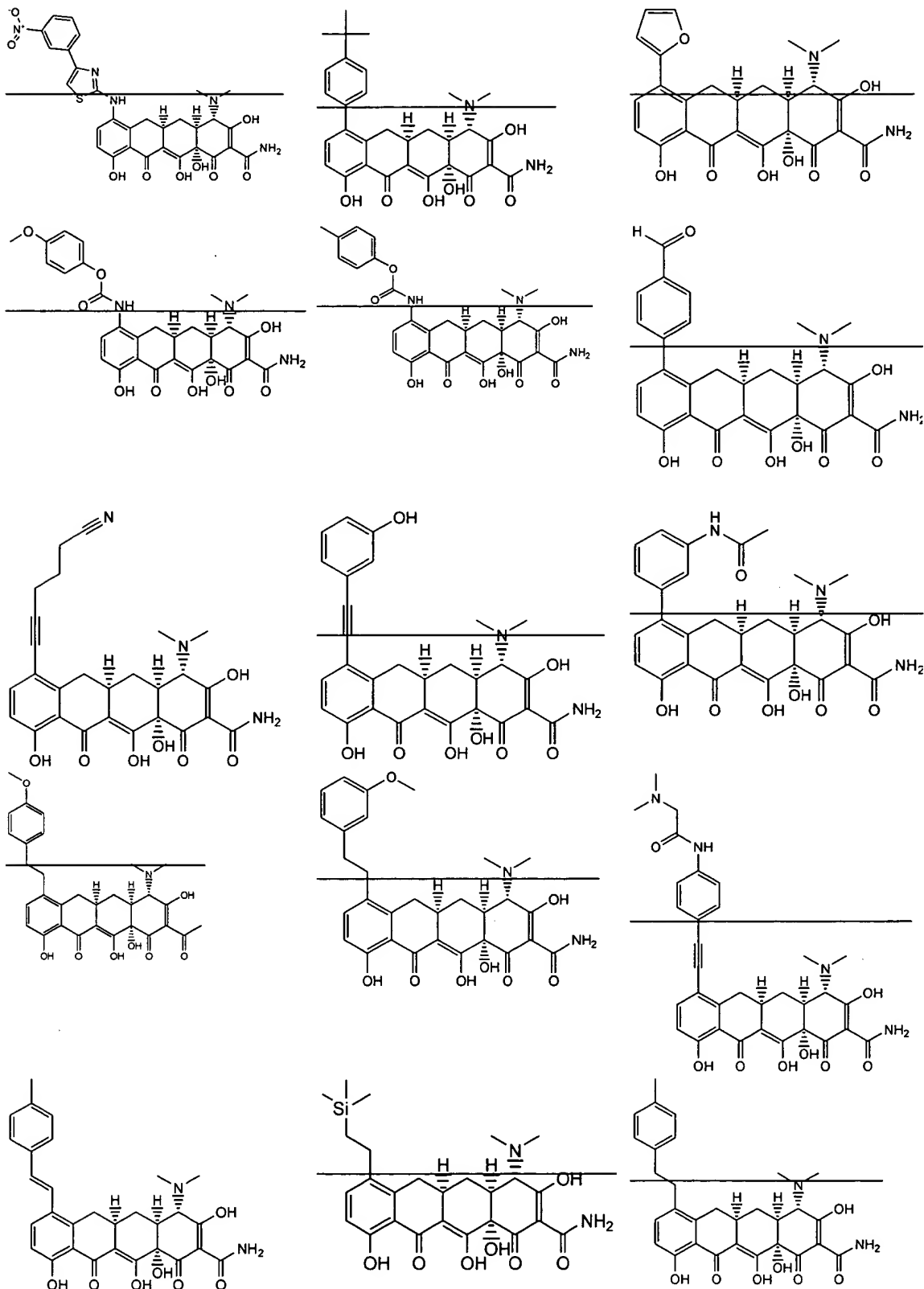
$\text{R}^8$  is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

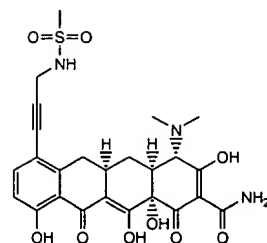
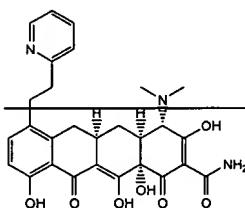
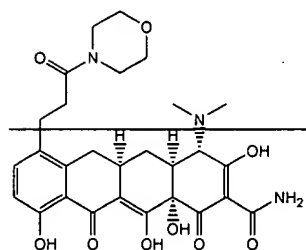
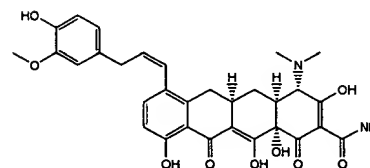
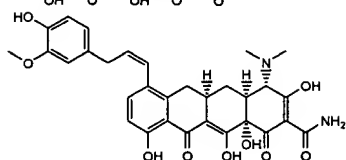
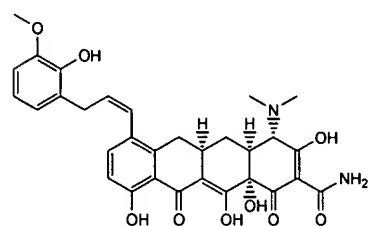
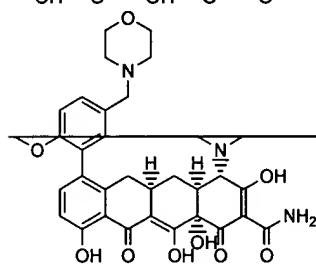
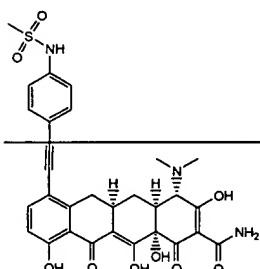
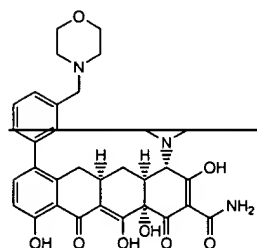
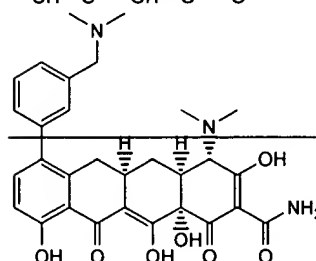
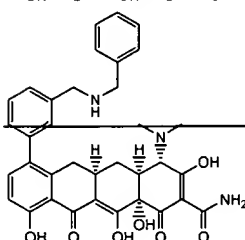
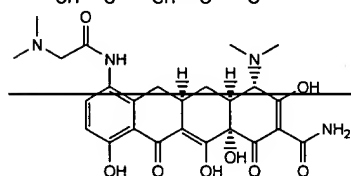
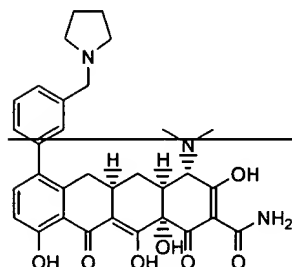
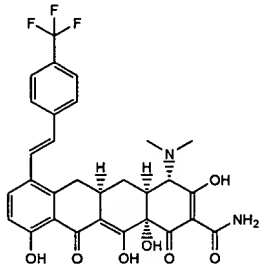
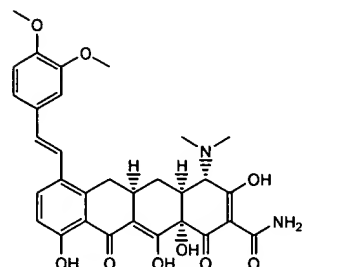
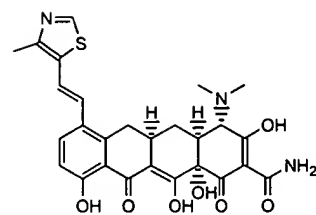
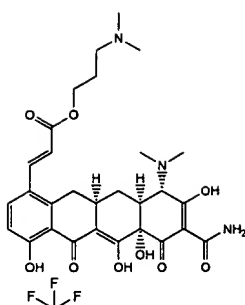
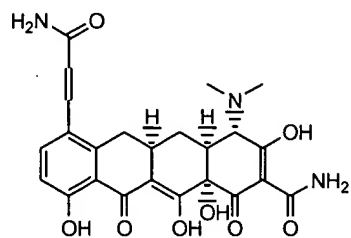
$\text{R}^{13}$  is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and

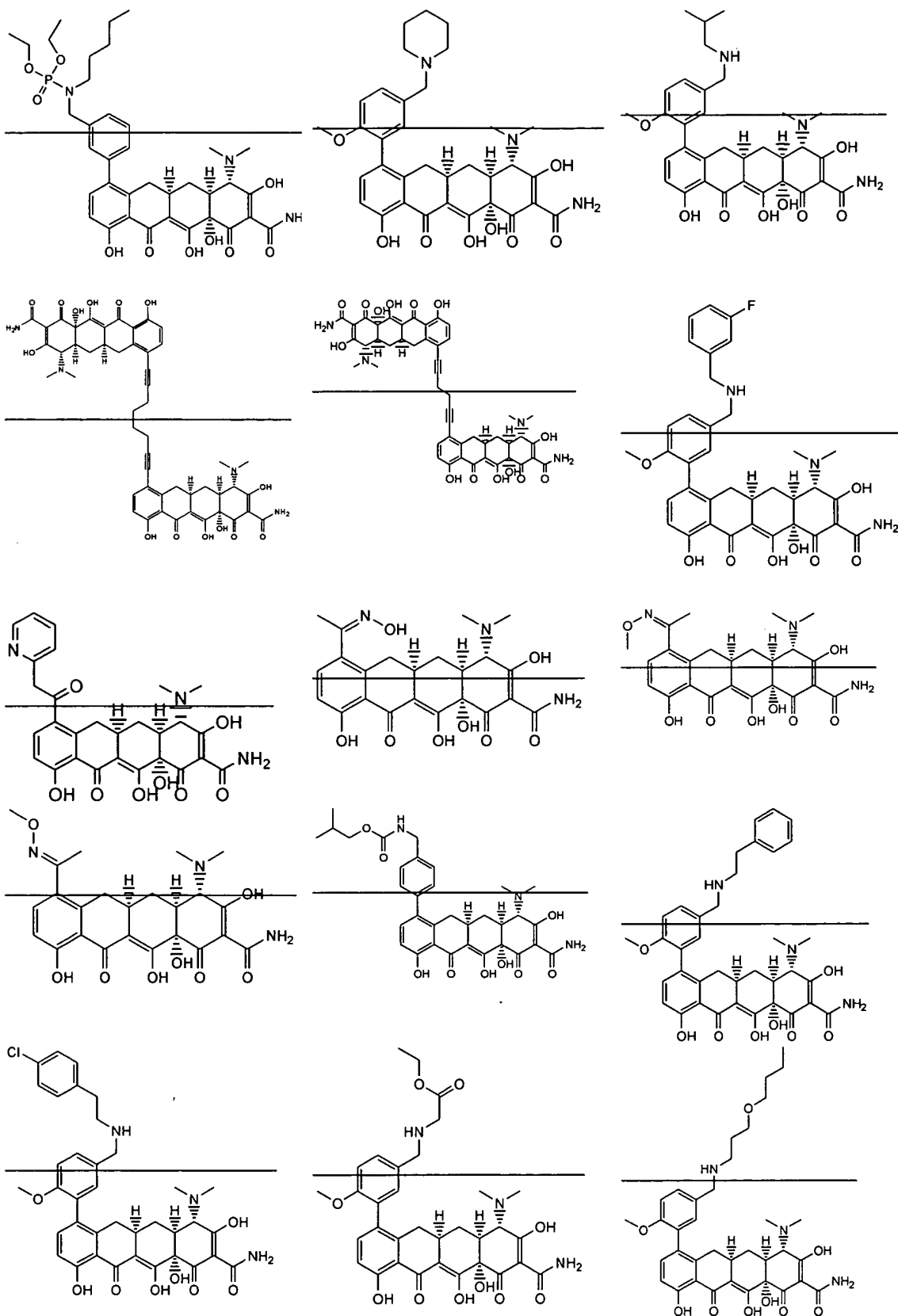
$\text{Y}'$  and  $\text{Y}$  are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl, and pharmaceutically acceptable salts thereof.

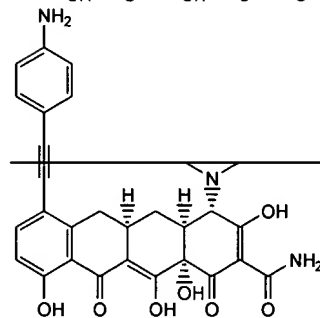
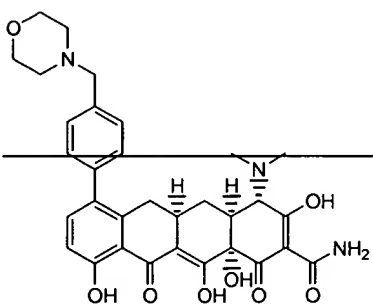
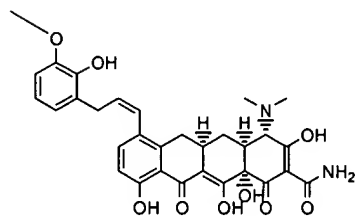
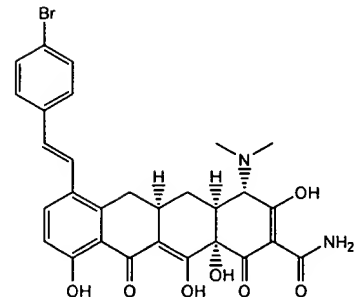
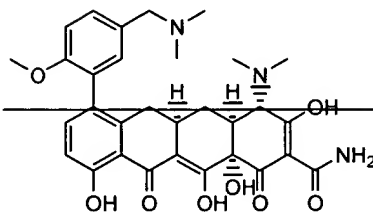
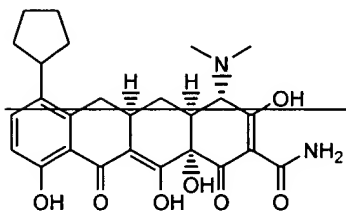
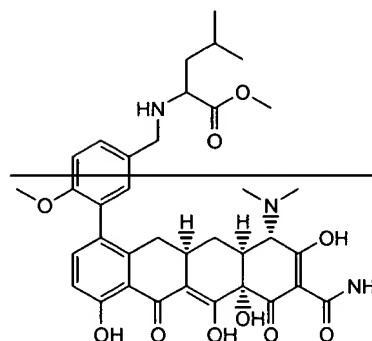
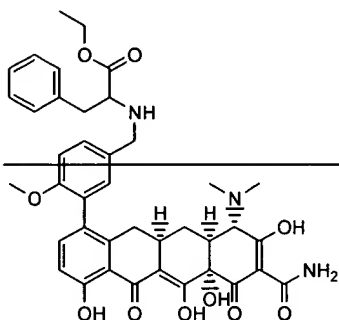
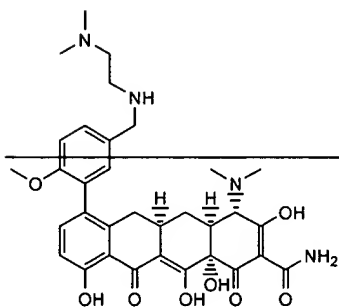
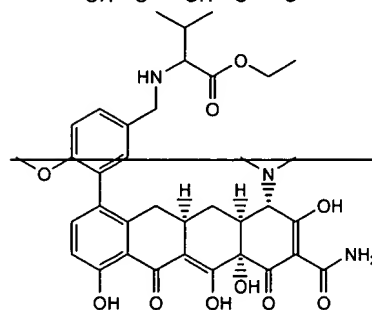
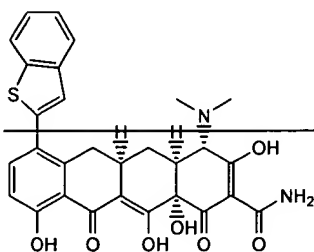
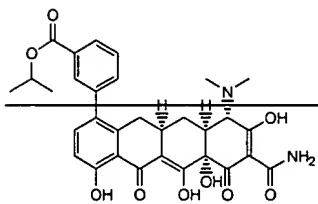
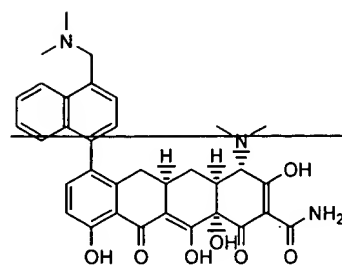
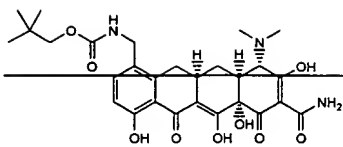
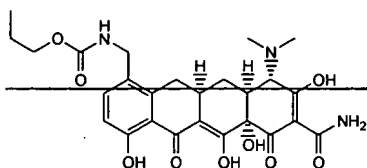
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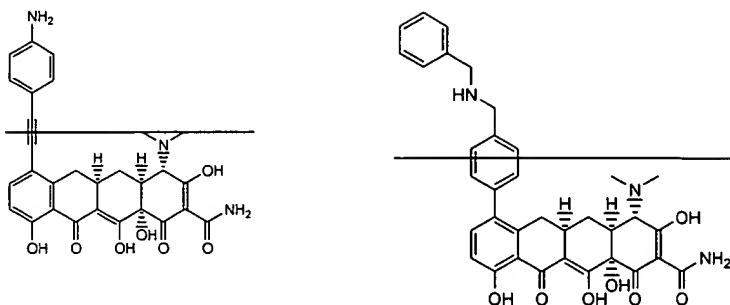
Claim 71 (currently amended): A tetracycline compound selected from the group consisting of:











and pharmaceutically acceptable salts, prodrugs and esters thereof.

Claims 72-73 (cancelled).

Claim 74 (currently amended): The compound of claim 1, 56, or 71, wherein said compound is at least 75% free of positional isomers.

Claim 75 (original): The compound of claim 74, wherein said compound is at least 80% free of positional isomers.

Claim 76 (original): The compound of claim 75, wherein said compound is at least 85% free of positional isomers.

Claim 77 (original): The compound of claim 76, wherein said compound is at least 90% free of positional isomers.

Claim 78 (original): The compound of claim 77, wherein said compound is at least 95% free of positional isomers.

Claim 79 (currently amended): A method for treating a tetracycline responsive state in a subject, comprising administering to said subject a tetracycline compound of any one of claims 1-3, 53-56, 71, 87, or 89-97, such that said subject is treated.

Claim 80 (original): The method of claim 79, wherein said tetracycline responsive state is a bacterial infection.

Claim 81 (original): The method of claim 80, wherein said bacterial infection is associated with *E. coli*.

Claim 82 (original): The method of claim 80, wherein said bacterial infection is associated with *S. aureus*.

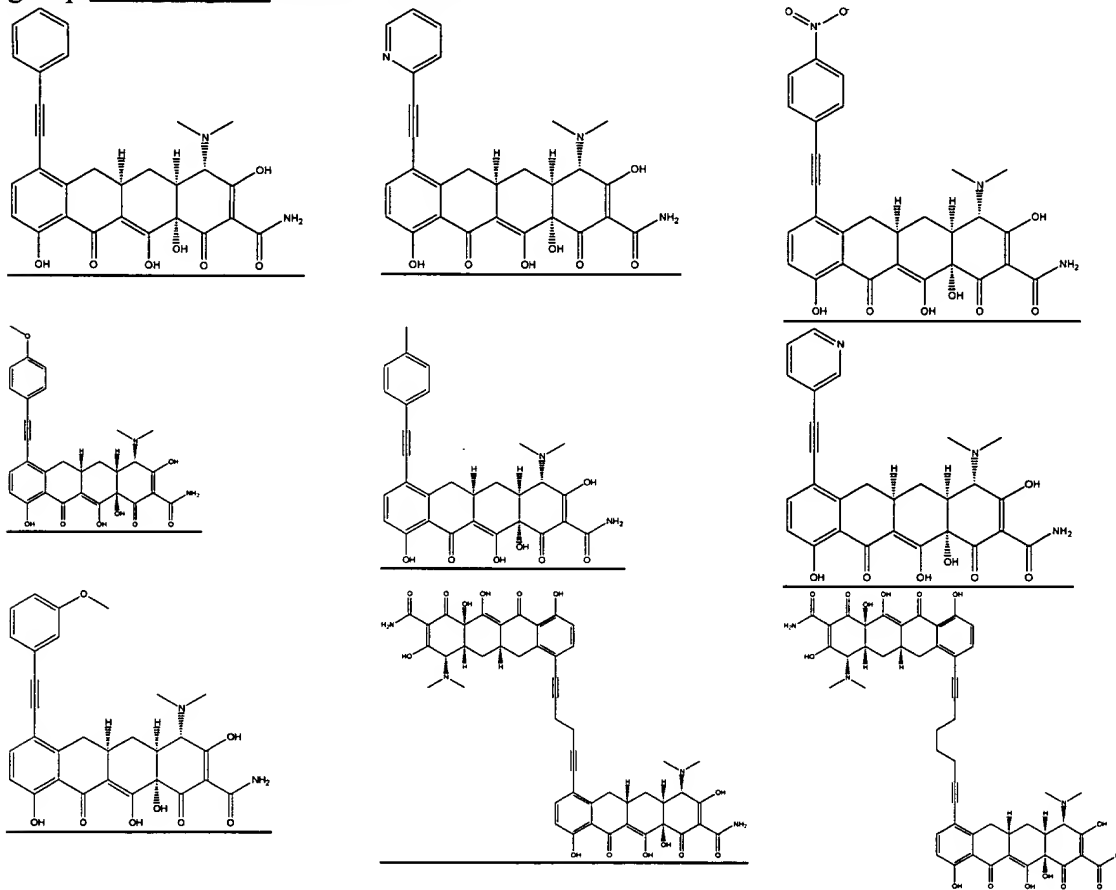
Claim 83 (original): The method of claim 80, wherein said bacterial infection is associated with *E. faecalis*.

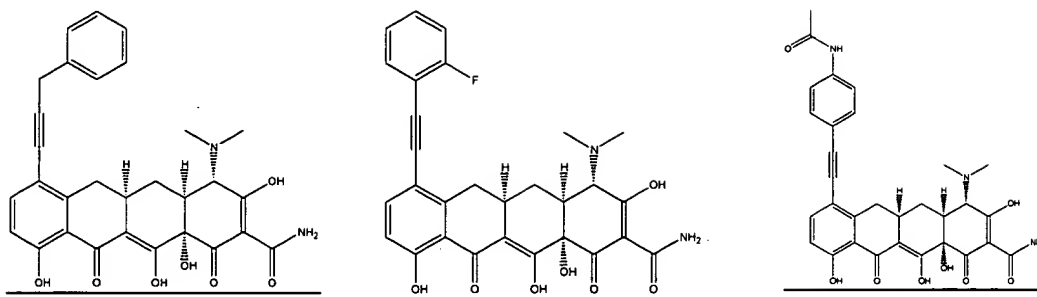
Claim 84 (original): The method of claim 80, wherein said bacterial infection is resistant to other tetracycline antibiotics.

Claim 85 (original): The method of claim 79, wherein said subject is a human.

Claim 86 (original): The method of claim 79, wherein said tetracycline compound is administered with a pharmaceutically acceptable carrier.

Claim 87 (currently amended): A substituted tetracycline compound selected from the group consisting of: ~~listed in Table 2.~~

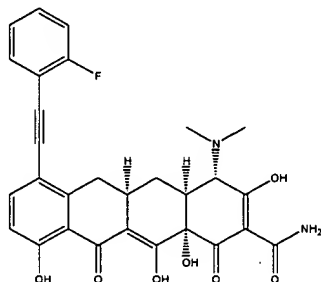




and pharmaceutically acceptable salts, esters and prodrugs thereof.

Claim 88 (currently amended): A pharmaceutical composition comprising a therapeutically effective amount of a tetracycline compound of claim 1-3, 53-56, 71, or 87, or 89-97 and a pharmaceutically acceptable carrier.

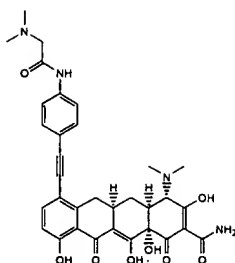
Claim 89 (previously presented): The substituted tetracycline compound of claim 87, wherein said compound is



Claim 90 (New): The substituted tetracycline compound of claim 1, wherein R<sup>9</sup> is alkynyl substituted with a heteroaryl group.

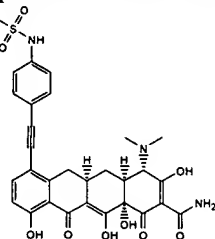
Claim 91 (New): The substituted tetracycline compound of claim 90, wherein said heteroaryl group is pyrrole, furan, thiophene, thiazole, isothiazole, imidazole, triazole, tetrazole, pyrazole, oxazole, isooxazole, pyridine, pyrazine, pyridazine, pyrimidine, benzoxazole, benzodioxazole, benzothiazole, benzoimidazole, benzothiophene, quinoline, isoquinoline, naphthridine, indole, benzofuran, purine, benzofuran, deazapurine, or indolizine.

Claim 92 (New): A tetracycline compound of the formula:



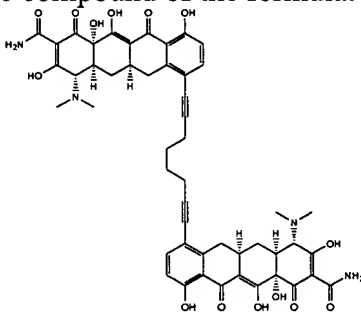
and pharmaceutically acceptable salts, prodrugs and esters thereof.

Claim 93 (New): A tetracycline compound of the formula:



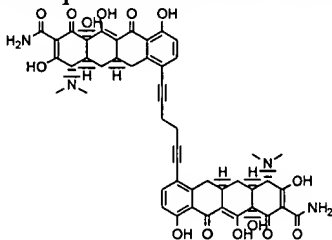
and pharmaceutically acceptable salts, prodrugs and esters thereof.

Claim 94 (New): A tetracycline compound of the formula:



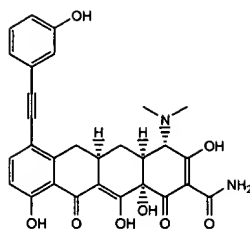
and pharmaceutically acceptable salts, prodrugs and esters thereof.

Claim 95 (New): A tetracycline compound of the formula:



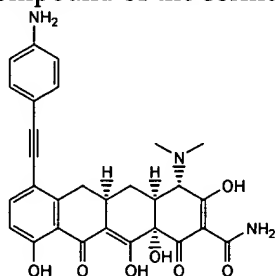
and pharmaceutically acceptable salts, prodrugs and esters thereof.

Claim 96 (New): A tetracycline compound of the formula:



and pharmaceutically acceptable salts, prodrugs and esters thereof.

Claim 97 (New): A tetracycline compound of the formula:



and pharmaceutically acceptable salts, prodrugs and esters thereof.